REMARKS

I. Introduction – Claim Status

This amendment under 37 C.F.R. §§1.111 is submitted in response to the outstanding Office Action of March 13, 2001, and is accompanied by a Petition for Extension of Time with fee. The Office Action indicates that claims 1-12 are now pending, and claims 13-21 are withdrawn from further consideration, in view of a Final Restriction Requirement set forth in the Office Action. Applicant hereinbelow respectfully submits that the Final Restriction Requirement is improper and thus, that claims 13-21 should also be subject to consideration on the merits. In the present amendment, claims 6-11 are herein amended merely for additional clarity. Applicant submits that these amendments are neither narrowing amendments nor made for reasons of patentability. Applicant respectfully requests reconsideration in view of the herewith presented amendments and remarks.

II. The Final Restriction Requirement

The Office Action of November 9, 1999, set forth a Final restriction requirement under 35 U.S.C., §121 to Group I of the following inventions:

I. Claims 1-12, drawn to a diagnostic system comprising different analyzers for performing biological marker measurements, classified in class 422, for example.

II. Claims 13-15, drawn to a computer program and computer readable medium, classified in class 266, subclass 80, for example.

III. Claims 16-21, drawn to method of using automated diagnostic system and

apparatus, classified in 128, subclass 632, for example.

In their response to the 11/9/99 Office Action, Applicant respectfully submitted that the Final Restriction Requirement was improper, and should be withdrawn for reasons elaborated in Applicant's 9/27/99 response to the original restriction requirement (emphasis added):

> [T]o the extent that a proper restriction requirement *has been or will be* made, however, Applicant respectfully traverses such requirement on the grounds that the inventions are obvious over each other within the meaning of 35 USC § 103. Accordingly, as indicated in MPEP §803, restriction should not be required. *In re Lee*, 199 USPQ 108 (Comm'r Pat. 1978).

Yet, in the instant Office Action, the Final Restriction Requirement is maintained because "[t]he record set forth in the previous restriction requirement clearly indicated that the delineated inventions are in fact patentably distinct each from the other or independent from the other [and thus] [t]he requirement is still deemed proper and is therefore made FINAL for the reasons of record."

Applicant respectfully requests reconsideration and withdrawal of the restriction requirement based on the examination guidelines set forth in MPEP §803. Particularly, if the Examiner maintains the restriction, Applicant respectfully requests that the Examiner elaborate how such a position is consistent with the examination procedures set forth in MPEP §803.

III. The 35 U.S.C. §112, ¶2 Rejections

Claims 6-12 are rejected under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Office Action identifies specific language believed to render the claims indefinite.

Regarding claim 6, the Office Action asserts that "wherein said processor supports the diagnosis of the pathology" is indefinite because it is unclear what is encompassed by the term "supports". While Applicant maintains that this language is clear and definite in light of the specification, Applicant has nevertheless amended claim 6 in a manner that does not narrow the claim, but merely provides additional clarity. As may be appreciated, the language of claim 6 clearly indicates that it embraces, *inter alia*, the processor providing "diagnostic information on the pathology".

Regarding claim 7, the Office Action asserts (citing MPEP §2173.05(d)) that "additional stored information" renders the claim indefinite because the claim includes elements not actually disclosed (those encompassed by "additional"), thereby rendering the scope of the claim unascertainable.

Applicants respectfully traverse this rejection on the grounds that the use of the terminology "additional stored information" is not indefinite to an ordinarily skilled artisan in light of the specification. The claim language plainly means that the "diagnosis of the pathology" is not necessarily exclusively based on the "results from the measurements executed according to said reflex algorithm" but also may depend on "additional stored information concerning the subject". Applicant submits that in light of the specification, one skilled in the art understands that this "additional stored information" may include any of myriad other factors (e.g., family history, other test results, etc., preferably stored in a database). See, e.g., specification at p. 14, ll. 1-6.

Applicant further notes that the Office Action's reliance on MPEP §2173.05(d) is inapposite inasmuch as this section is directed to numerical ranges and amount limitations, *viz.*,

purely quantitative limitations. While Applicant recognizes that "additional stored information" may be considered as relating to a "quantity" of information depending on how many other factors this information represents, it does not refer to a purely quantitative limitation inasmuch as it refers to various information different in kind from the "results from the measurements executed according to said reflex algorithm". Further, Applicant submits that to the extent that this MPEP section may have some relation to the "additional stored information", it in fact supports Applicant's position that this language is definite to those skilled in the art. More specifically, MPEP §2173.05(d) states, in part, as follows (emphasis added):

> The common phrase "an effective amount" may or may not be indefinite. The proper test is whether or not one skilled in the art could determine specific values for the amount based on the disclosure. See In re Mattison, 509 F.2d 563, 184 USPQ 484 (CCPA 1975). *The phrase "an effective amount . . . for growth stimulation" was held to be definite where the amount was not critical and those skilled in the art would be able to determine from the written disclosure, including the examples, what an effective amount is.* In re Halleck, 422 F.2d 911, 164 USPQ 647 (CCPA 1970). The phrase "an effective amount" has been held to be indefinite when the claim fails to state the function which is to be achieved and more than one effect can be implied from the specification or the relevant art. In re Fredericksen 213 F.2d 547, 102 USPQ 35 (CCPA 1954). *The more recent cases have tended to accept a limitation such as "an effective amount" as being definite when read in light of the supporting disclosure and in the absence of any prior art which would give rise to uncertainty about the scope of the claim. In Ex parte Skuballa, 12 USPQ2d 1570 (Bd. Pat. App. & Inter. 1989), the Board held that a pharmaceutical composition claim which recited an "effective amount of a compound of claim 1" without stating the function to be achieved was definite, particularly when read in light of the supporting disclosure which provided guidelines as to the intended utilities and how the uses could be effected.*

Applicant's claim 6 clearly states that the function or purpose achieved by the "additional stored information" together with the "results from the measurements executed

according to said reflex algorithm" is to provide information which contributes to the diagnosis of the pathology. Additionally, Applicant submits that in light of the specification, those skilled in the art understand that the precise amount of "additional stored information" is not critical, provided the information contributes to the diagnosis of the pathology. Indeed, the supporting disclosure not only provides illustrative examples of "additional stored information", but also elaborates its function, purpose, or intended use. See, e.g., specification at p. 14, ll. 1 et seq. Accordingly, Applicant respectfully submits that in light of the specification, an ordinarily skilled artisan understands the scope and meaning of claim 6, which is not limited to specific ones or some specific amount of "additional stored information", but includes any such information that contributes to the diagnosis of the pathology.

While for at least these reasons Applicant maintains that claim 6 is clear and definite in light of the specification, Applicant has nevertheless amended claim 6 in a manner that does not narrow the claim, but nonetheless provides additional clarity.

The Office Action maintains that claim 8 remains indefinite for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. More particularly, the Office Action asserts that claim 8 "fails to specify what element in the hematology analyzer communicates with the processor so as to enable it to respond and execute specific commands." Applicant respectfully traverses this rejection.

Applicant submits that the claim recites a structural relationship between the hematology analyzer and the processor in a manner such that the scope of the claim is clear and unambiguous to one of ordinary skill in the art. That is, the recitation that a "hematology

analyzer [is] coupled to said processor" such that hematology measurements are "executed by the hematology analyzer in response to a command from said processor" clearly delimits a structural relationship. Indeed, those skilled in the art understand that there are various ways a processor may be structurally coupled to a hematology analyzer such that the hematology analyzer executes measurements in response to a command from the processor. Moreover, those skilled in the art will further appreciate that the description in the specification concerning various structural implementations for a processor to control immunoassay and/or clinical chemistry measurements may be applied to coupling a hematology analyzer to a processor to control hematology measurements. See, e.g., p. 18, l. 23 et seq. Accordingly, for at least these reasons, Applicant respectfully submits that, in light of the specification, the scope of claim 8 is clear and definite. Nevertheless, claim 8 has been amended for additional clarity without narrowing the claim.

Regarding claims 9 and 10, Applicant submits that "including" does not render the claim indefinite in light of the specification; however, Applicant has amended the claim to provide additional clarity based on the Examiner's suggestion. In any event, Applicant submits that in light of the specification, the claim clearly delimits that the biochemical marker measurement steps include an immunoassay measurement and a clinical chemistry assay measurement (i.e., the sequence of biochemical measurement steps include at least one immunoassay measurement and at least one clinical chemistry assay measurement), and any given biochemical measurement step may be at least one immunoassay measurement or at least one clinical chemistry assay measurement or a combination thereof. Further, Applicant submits that the claim clearly delimits that each of the biochemical marker measurement steps includes (but is not limited to) measuring an appropriate characteristic (i.e., concentration or activity) of at

least one biochemical marker in any one of or any combination of a urine, serum, plasma, or whole blood sample.

Although Applicant maintains that claim 11 is definite, Applicant has nevertheless amended this claim for additional clarity based on the Examiner's comments. Thus, the § 112, ¶2 of claim 11 is obviated and rendered moot.

Applicant respectfully submits that claim 12 is clear in light of the specification, (see, e.g., page 18, l. 23 et seq.), and embraces an embodiment in which the first and second processors are local processors that communicate with "said processor".

In view of the foregoing, Applicants respectfully submit that the rejections of claims 6-12 under 35 U.S.C. §112, second paragraph, should be withdrawn.

IV. The 35 U.S.C. §112, ¶1 Rejections

The Office Action reasserts the rejection of claims 1-12 under 35 USC 112, first paragraph, based on the assertion that the specification, while being enabling for acute myocardial infarction biochemical markers, does not reasonably provide enablement for other biochemical markers, such as thyroid profile markers and hepatitis profile markers. It further asserts that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. More specifically, the 11/9/99 Office Action sets forth the following reasoning:

> As to the biochemical markers, the direction and guidance in the specification is notably limited to specific acute myocardial infarction markers, such as total creatine kinase, myoglobin, troponin I, etc. The working examples, likewise are limited to the cardiac markers. Based on this limited disclosure and direction, one of the skill in the art would not

> know how to use alternative biochemical markers, such as thyroid profile markers in the instant diagnostic system which comprise immunoassay analyzer, clinical chemistry analyzer, and hematology analyzer, without undue experimentation.

As previously argued, Applicant respectfully maintains that the specification clearly and completely describes the invention such that an ordinarily skilled artisan would know how to make and/or use the claimed invention without undue experimentation. That is, an ordinarily skilled artisan would know how to make and use Applicant's claimed invention (e.g., the apparatus of claim 1) such that the program would implement any reflex algorithm that may be developed and which includes both immunoassays and clinical chemistry assays to diagnose pathology. To limit the scope of Applicant's claimed diagnostic system (e.g,, that includes, *inter alia*, an immunoassay analyzer integrated with a clinical chemistry analyzer under control of a reflex algorithm) to only systems that implement reflex algorithms expressly disclosed in the specification (or that are already known in the art) unduly and improperly limits Applicant's claimed invention. Moreover, Applicant respectfully submits that implementing the Applicant's system as claimed, but using other to-be-developed reflex algorithms, would not require undue experimentation. Accordingly, Applicant submits that the specification clearly enables the claimed invention, and thus requests withdrawal of the rejection under 35 U.S.C. §112, first paragraph.

V. The 35 U.S.C. §103(a) Rejections

The Office Action also maintains the rejection of claims 1-12 under 35 USC 103(a) as being unpatentable over Lillig et al. (US 4,965,049) in view of Groth et al. (US 5,690,103) and in further view of Furlong et al. (Clinical Chemistry, 1990), based on the reasons

of record.

Applicant maintains that even assuming *arguendo* that Lillig, Groth, and Fulong, may be combined as asserted in the office action, the combination fails to provide Applicant's claimed invention as a whole, and there is no motivation or suggestion for modifying the combination to provide Applicant's claimed invention as a whole.

As may be appreciated, Applicant's claimed invention (claim 1) is directed to a diagnostic system that includes an immunoassay analyzer, a clinical chemistry analyzer, and an automatic sample handling device coupled between the immunoassay analyzer and the clinical chemistry analyzer to allow sharing of samples therebetween. A processor communicates with the immunoassay analyzer and the clinical chemistry analyzer, wherein the processor commands the immunoassay analyzer and clinical chemistry analyzer to execute measurements specified by a program executed by the processor in order to facilitate diagnosis of a pathology for a subject according to a reflex algorithm which includes at least one immunoassay and at least one clinical chemistry assay. Additionally, Applicant's invention of claim 9 is directed to a system for executing a sequence of biochemical marker measurement steps, including immunoassay and clinical chemistry assay measurements, to generate an indication of a pathology, the system including means for selectively commanding an immunoassay measurement means and a clinical chemistry assay means to perform specified biochemical marker measurements according to a reflex algorithm.

More specifically, Applicant respectfully submits that Lillig, Groth, and Furlong, even if combined as asserted in the Office Action, do not provide all the limitations of Applicant's claimed invention, and further one skilled in the art would not have been motivated to modify such

a combination to provide Applicant's claimed invention as a whole, which includes, *inter alia*, an immunoassay analyzer and a clinical chemistry assay analyzer that are controlled according to "reflex algorithm".

As explained in Applicant's specification (see, e.g., p. 2, l. 14 et seq.), a reflex algorithm refers to an algorithm in which the selection/performance of a subsequent test is based on results of previous tests, without the need for subjective human decision-making in selecting tests, and thus the diagnostic indication or determination and the sequence of tests performed are thus inter-related..

As previously explained, consonant with the 11/9/99 Office Action's statement that Lillig et al. "fail[] to teach diagnostic nature of the modular analyzer system. . . . [and] are silent in the teaching of analyte assays and thereby, fail to disclose analysis of biochemical markers", Applicant submits that the Lillig et al reference relates to a modular clinical chemistry analyzer and neither discloses nor suggests performing tests on the modular analyzer according to a "reflex algorithm".

As Applicant previously explained, Groth and Furlong each relates to neural network analysis of biochemical marker measurements to classify patients suspected of having acute myocardial infarction (AMI). Such neural network analysis provides classification based on inputs from results of a set of biochemical marker measurements taken at certain time intervals. The neural network has been previously trained based on a training sample set, and the results of the biochemical marker measurements are input into the neural network, which then outputs an indication of AMI. This neural network paradigm is in stark contrast to a reflex algorithm as claimed by Applicant's, at least to the extent that the neural network classifies

according to a predetermined set of biochemical marker measurements (the results of which are all input into the neural network).

In response to Applicant's arguments filed 5/10/00 that the neural network taught by both Groth and Furlong is in stark contrast to Applicant's claimed reflex algorithm, the Office Action asserts the following:

> Contrary to Applicant's argument, the "reflex algorithm" as claimed in the instant invention is an inherent property of neural network design disclosed by prior art because neural networks provide for feedback mechanism which further provides for a decision and suggestion to perform other activity or to activate another network structure which Groth refers to as a "feedback connection from conclusive diagnostic unit" (see column 16, lines 42-67) so that further testing, if desired, can be activated into preprogrammed analytical computer software to further analyze a blood sample. Incorporation of such a capability is an obvious design choice to one of ordinary skill, taing advantage of neural network capacity to provide feedback mechanism to further activate "function" into another neural structure, in this case, to pursue further subsequent testing by the analyzer.

Nevertheless, even Groth's disclosure of the feedback structure employing neural networks in Figure 17 is in stark contrast to a reflex algorithm as claimed. More specifically, as understood by Applicant, if the first neural network structure 224 (together with the conclusive diagnostic unit 226) generates a non-diagnosis indication, then the identical set of biochemical marker measurements are run at a later time and the second neural network classifies the results based on the temporal pattern of these later obtained biochemical marker measurements. Thus, since this structure simply provides selectively repeating the identical set of markers at a later time, and nonetheless *determines AMI* according to classification by a trained neural network structure operating on all the marker measurements, it cannot be said to provide a reflex

algorithm wherein which (if any) subsequent biochemical marker measurement is performed depends upon the results of previous measurements, and the *indication and sequence of tests performed are thus inter-related.* Simply stated, the feedback structure shown in Figure 17 of Groth does not transform the classification by a neural network into a determination according to a reflex algorithm as claimed. (Again, Applicant respectfully notes that the background section of Applicants' specification provides additional background information contrasting neural network techniques and reflex algorithm techniques.)

Moreover, Applicant submits that Groth an Furlong, in fact, teach away from Applicant's claimed invention inasmuch as such a neural network paradigm (regardless of feedback or repetition) is directed to classification based on a pre-determined, immutable set of measurements that are fed into a trained neural network for classification, which is diametric to a reflex algorithm wherein determination of a pathology is associated with different possible measurement sequences.

Thus, for at least these reasons, Applicants respectfully submit that even assuming arguendo that Lillig, Groth, and Furlong may be combined as asserted in the Office Action, such a combination would fail to teach all the limitations of Applicant's claimed invention, and there would have been no motivation or suggestion to modify such a combination to provide Applicant's claimed invention as a whole. Accordingly, Applicant respectfully requests that the §103(a) rejection of claims 1-12 be withdrawn.

VI. Conclusion

In view of the above amendments and remarks, Applicants respectfully submit that the application is in condition for allowance. Reconsideration and withdrawal of the Examiner's rejections is respectfully requested and allowance of all pending claims is respectfully submitted.

If any outstanding issues remain, or if the Examiner has any suggestions for expediting allowance of this application, the Examiner is invited to contact the undersigned at the telephone number below.

The Examiner's consideration of this matter is gratefully acknowledged.

Respectfully submitted,

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CLAIM AMENDMENT ANNEX

6. (Amended) The diagnostic system according to claim 1, wherein said processor [supports] provides information that facilitates the diagnosis of the pathology.

7. (Twice Amended) The diagnostic system according to claim 1, wherein the diagnosis of the pathology for the subject is based, at least in part, on results from the measurements executed according to said reflex algorithm and on additional stored information concerning the subject, the additional stored information being different from the results from the measurements executed according to said reflex algorithm.

8. (Twice Amended) The diagnostic system according to claim 1, further comprising a hematology analyzer coupled to said processor, and wherein the program further specifies hematology measurements to be executed by the hematology analyzer in response to the hematology analyzer receiving a command from said processor.

9. (Twice Amended) A system for executing a sequence of biochemical marker measurement steps to generate an indication of a pathology, the biochemical marker measurement steps including an immunoassay measurement and a clinical chemistry assay measurement, each of the biochemical marker measurement steps [including] comprising measuring at least one [a] concentration level or [an] activity of at least one biochemical marker in at least one of a urine, serum, plasma or whole blood sample, the system comprising:

means for performing an immunoassay measurement;

means for performing a clinical chemistry assay measurement;

means for sample handling between the immunoassay measurement means and the clinical chemistry assay measurement means;

means for storing information representing a reflex algorithm indicating a plurality of predetermined sequences of biochemical marker measurements;

means for receiving information concerning outputs from biochemical marker measurements conducted on the immunoassay means and the clinical chemistry assay means;

means for selectively commanding said immunoassay measurement means and said clinical chemistry assay means to perform a specified biochemical marker measurement according to said reflex algorithm; and

means for specifying an indication of the pathology according to the stored information in response to the information concerning outputs from biochemical marker measurements.

10. (Twice Amended) A system for executing a sequence of biochemical marker measurement steps, the biochemical marker measurement steps including immunoassay and clinical chemistry assays, each of the biochemical marker measurement steps [including] comprising measuring at least one [a] concentration level or [an] activity of at least one biochemical marker in at least one of a serum, plasma or whole blood sample obtained from a subject at a time specified by a reflex algorithm, the system comprising:

immunoassay instrumentation that allows automatic execution of an immunoassay measurement;

clinical chemistry instrumentation that allows automatic execution of a clinical chemistry assay measurement;

a sample handling device coupled between said immunoassay instrumentation and said clinical chemistry instrumentation to allow sharing of samples therebetween;

a computer-readable medium that stores information that represents the reflex algorithm; and

a processor coupled to said immunoassay instrumentation, said clinical chemistry instrumentation, and said computer-readable medium, wherein said processor receives information representative of outputs from biochemical marker measurements conducted on the immunoassay instrumentation and on the clinical chemistry instrumentation, and selectively commands said immunoassay instrumentation and said clinical chemistry instrumentation to execute the biochemical marker measurement according to the reflex algorithm.

11. (Twice Amended)The system according to claim 10, wherein said processor selectively

provides a suggested diagnostic indication of a pathology according to the reflex algorithm in response to receiving the information representative of outputs from biochemical marker measurements.